

Fostnotes

Footnotes

1. Footnote 1. <http://www.cfsan.fda.gov/~dms/nuttf-e.html>
2. Footnote 2. A meta-analysis is the process of systematically combining and evaluating the results of clinical trials that have been completed or terminated (Spilker, 1991, p. 793).
3. Footnote 3. The Osteoarthritis Initiative (OAI) is sponsored by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute of Health, Department of Health and Human Services (<http://www.niams.nih.gov/ne/oi/>)
4. Footnote 4. See <http://www.fda.gov/ohrms/dockets/ac/cfsan04.html> for FAC transcripts and other meeting information.
5. Footnote 6. Guidance for Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements, December 22, 1999. <http://www.cfsan.fda.gov/~dms/ssaguide.html>
6. Footnote 7. Eburnation is a change in exposed subchondral bone in degenerative joint disease in which subchondral bone is converted into a dense substance with a smooth surface like ivory (Stedman's Medical Dictionary).
7. Footnote 8. An osteophyte is a bony outgrowth or protuberance (Stedman's Medical Dictionary).
8. Footnote 9. <http://www.rheumatology.org/public/factsheets/oa.asp?aud=pat>
9. Footnote 10. See the Prospectus of the OA Initiative at <http://www.niams.nih.gov/ne/oi/>
10. Footnote 13. <http://www.clinicaltrials.gov/show/NCT00032890>
11. Footnote 14. <http://clinicaltrials.gov/show/NCT00086229>
12. Footnote 15. <http://ntp-server.niehs.nih.gov/NomPage/2003Noms.html>
13. Footnote 26. Chondropathia patellae is a disease of the cartilage and patella (Stedman's Medical Dictionary and Dorland's Illustrated Medical Dictionary). The patella is a bone in the knee commonly referred to as the kneecap.
14. Footnote 33. A chondrocyte is a non-dividing cartilage cell occupying a lacuna (i.e., small space or cavity) within the cartilage matrix (Stedman's Medical Dictionary).
15. Footnote 37. A cytokine is a generic term for nonantibody proteins released by one cell population on contact with specific antigen, which act as intercellular mediators, as in the generation of an immune response (Dorland's Illustrated Medical Dictionary).
16. Footnote 56. A meta-analysis is the process of systematically combining and evaluating the results of clinical trials that have been completed or terminated (i.e., primary reports) (Spilker, 1991, p. 793). FDA uses meta-analysis to identify relevant primary reports, which the Agency then evaluates.
17. Footnote 58. The background section of the FAC questions document (http://www.fda.gov/ohrms/dockets/ac/04/briefing/4045b1_06_a_Questions%20Revised.pdf) stated that FDA also refers to modifiable risk factors/surrogate endpoints for disease as "biomarkers" and further explained, in part, that a biomarker is "a measurement of a variable related to a disease that may serve as an indicator or predictor of that disease. Biomarkers are parameters from which the presence or risk of a disease can be inferred, rather than being a measure of the disease itself. In conducting a health claim review, FDA does not rely on a change in a biomarker as a

measurement of the effect of a dietary factor on a disease unless there is evidence that altering the parameter can affect the risk of developing that disease or health-related condition.” See also the discussion of modifiable risk factors in the introduction to section I.B.1.

18. Footnote 61. <http://www.cfsan.fda.gov/~dms/ds-ltr11.html>